Constructing 3D interaction maps from 1D epigenomes.

Journal: Nat Commun

Publication Year: 2016

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PubMed link: 26960733

Funding Grants: Systems-level discovery of the regulatory mechanisms directing differentiation of hESC

Public Summary:
The chromatin structure plays a crucial role in regulating gene expression and the spatial contacts between gene promoters and enhancers change during differentiation of embryonic stem cells. Therefore, it is important to understand the relationship between the 3D chromatin structure and epigenetic modifications in the human embryonic stem cells and the early developmental cells. We have developed a novel bioinformatics method to decipher this relationship and applied to the H1 embryonic stem cell and four H1-derived cells representing different lineages. Our study revealed the possibility of predicting 3D chromatin interactions from the 1D epigenomic data and highlighted particular regions that are important for stabilizing the local 3D interactions. This work makes it possible to build a more precise network that can guide directed differentiation of embryonic stem cells to a specific lineage or differentiated cell types.

Scientific Abstract:
The human genome is tightly packaged into chromatin whose functional output depends on both one-dimensional (1D) local chromatin states and three-dimensional (3D) genome organization. Currently, chromatin modifications and 3D genome organization are measured by distinct assays. An emerging question is whether it is possible to deduce 3D interactions by integrative analysis of 1D epigenomic data and associate 3D contacts to functionality of the interacting loci. Here we present EpiTensor, an algorithm to identify 3D spatial associations within topologically associating domains (TADs) from 1D maps of histone modifications, chromatin accessibility and RNA-seq. We demonstrate that active promoter-promoter, promoter-enhancer and enhancer-enhancer associations identified by EpiTensor are highly concordant with those detected by Hi-C, ChIA-PET and eQTL analyses at 200 bp resolution. Moreover, EpiTensor has identified a set of interaction hotspots, characterized by higher chromatin and transcriptional activity as well as enriched TF and ncRNA binding across diverse cell types, which may be critical for stabilizing the local 3D interactions.